

#13
4-5-95



1546-0710

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Is re application of:

Cook et al.

Serial No.: 07/967,267

Group Art Unit: 1803


Filed: October 27, 1992

Examiner: G. Kunz

For: OLIGONUCLEOTIDES CONTAINING 2'-O-MODIFIED
PURINES

I, Paul K. Legaard, Registration No. 38,534 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On March 10, 1995


Paul K. Legaard Reg. No. 38,534

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

REQUEST FOR RECONSIDERATION

This responds the Office Action mailed November 10, 1994, in connection with the above-identified patent application, in which claims 9, 10, 15, and 16 are pending.

Claims 9 and 10 stand rejected under 35 U.S.C. § 101 and under 35 U.S.C. §112, first paragraph because the claimed compounds allegedly do not possess a patentable utility. Applicants respectfully request reconsideration of this rejection because there is no reason to believe that the claimed compounds cannot be used in diagnostics, therapeutics, and as research reagents, as taught by the specification. The Office Action's assertions to the contrary appear to find their origin in an incorrect assumption that the utility of the claimed compounds

"rests upon their specific hybridization potential." (Office Action at pages 2-3). However, there is no basis for limiting the utility of the claimed compounds in this manner. Persons skilled in the art would believe there to be numerous uses of the claimed compounds that do not involve hybridization. Also, the Office Action improperly suggests that, as to uses that do require hybridization, the claimed compounds will not hybridize. The only evidence provided in apparent support of this view is the teaching of Iribarren, *et al.*, *Proc. Natl. Acad. Sci. USA* 1990, 87, 7747, relating to bulky 2'-O-substituents.

Significantly, however, the Iribarren, *et al.* reference does not teach that compounds having bulky 2'-O-substituents do not hybridize, but, rather, that they do not hybridize as well as compounds that do not have such bulky substituents. Indeed, the reference's Abstract states that the single bulky group that was tested only "reduces" the compound's affinity. Since there is no reason to believe, in view of the Iribarren, *et al.* reference, that the claimed compounds will not hybridize to some measurable extent, such compounds must be deemed useful under the patent laws. Moreover, the published literature clearly indicates that the claimed compounds do, in fact, form sufficiently strong hybrids. For example, Guinosso, *et al.*, *Nucleosides & Nucleotides* 1991, 10(1-3), 259 (copy enclosed) discloses that compounds bearing rather bulky 2'-O-substituents such as 2'-O-nonyl groups form stable hybrids with complementary

oligonucleotides (see, e.g., Table 1 on page 260). Indeed, attachment of a 2'-O-nonyl group actually increased the melting temperature of the resulting hybrid. (*Id.*). Thus, reconsideration of the rejections under §§ 101 and 112 is requested.

Claims 9-10 stand rejected under 35 U.S.C. § 103 as being unpatentable over Cotten, *et al.*, *Nucleic Acids Research* 1991, 19(10), 2629, which is said to disclose "2'-O-ethyl containing oligoribonucleotides." (Office Action at page 5). Applicants traverse this rejection by demonstrating that they were in possession of the subject matter purportedly disclosed by the Cotten, *et al.* reference well before June 6, 1991, the date on which the reference appears to have become publicly available.¹

Enclosed herewith is a supplemental Declaration by the inventors claiming the priority benefit, pursuant to 35 U.S.C. §§ 120 & 363, of international patent application PCT/US91/00243 ("the 00243 Application"), which was filed January 11, 1991, designating the United States.² A copy of the 00243 Application, published as WO 91/10671, is enclosed herewith. WO

¹ Attached as Exhibit A is a copy of a March 2, 1995, letter from the Lehigh University Library, stating that the volume in which the Cotten, *et al.* reference appeared was received by the library on June 6, 1991.

² The 00243 Application has since entered the national phase in the United States and is pending as Application Serial No. 07/854,634, of which priority also is claimed.

91/10671 clearly demonstrates that Applicants had possession of "2'-O-ethyl containing oligoribonucleotides" by at least January 11, 1991, nearly five months before the date on which the Cotten, et al. reference was available. For example, WO 91/10671 at page 19, line 24 - page 20, line 4 discloses oligonucleotides containing at least one 2'-modified nucleoside unit, with O-alkyl groups having 1 to 12 carbons being a preferred modification. Thus, in view of the claim of priority evidenced by the accompanying supplemental Declaration, Applicants antedate the Cotten, et al. reference by showing prior reduction to practice of all the relevant disclosure of that reference (i.e., 2'-O-ethyl oligonucleotides) according to *In re Stryker*, 168 U.S.P.Q. 372 (C.C.P.A. 1971).

Claims 15 and 16 stand rejected under 35 U.S.C. § 103 as being unpatentable over the Iribarren, et al. reference in view of Wagner, et al., *Nucleic Acids Research* 1991, 19(21), 5965. The Office Action asserts that the Wagner, et al. reference discloses "2'-O-ethyl guanosine." (Office Action at page 7). Applicants traverse this rejection by claiming the priority benefit of the 00243 Application, which demonstrates that they were in possession of the subject matter purportedly disclosed by the Wagner, et al. reference by at least January 11, 1991, more than ten months before November 20, 1991, the date on

which the reference appears to have been publicly available.³ For example, WO 91/10671 at pages 19-20 discloses oligonucleotides consisting of guanine nucleic acid bases and at least one 2'-O-alkyl group having 1 to 12 carbon atoms. In view of this disclosure and the claim of priority evidenced by the accompanying supplemental Declaration, Applicants antedate the Wagner, *et al.* reference by showing prior reduction to practice of all the relevant disclosure of that reference (*i.e.*, 2'-O-ethyl guanosine) according to *In re Stryker*, 168 U.S.P.Q. 372 (C.C.P.A. 1971).

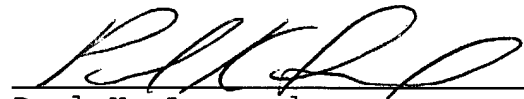
³ Attached as Exhibit A is a copy of a March 2, 1995, letter from the Lehigh University Library stating that the volume in which the Wagner, *et al.* reference appeared was received by the library on November 20, 1991.

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PATENT

In view of the foregoing, Applicants submit that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



Paul K. Legaard
Registration No. 38,534

Date: March 10, 1995

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EXHIBIT A
Lehigh University



*Information Service
Lehigh University Libraries*

*Mountaintop Campus
111 Research Drive
Bethlehem, Pennsylvania 18015-4732*

2 March 1995

Mr. Paul Legaard
Woodcock, Washburn, Kurtz,
Mackiewicz and Norris
1 Liberty Place
Philadelphia, PA 19103

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MAR 03 1995

**WOODCOCK WASHBURN
KURTZ MACKIEWICZ & NORRIS**

Dear Mr. Legaard:

Further to your request, I have located the editions of **NUCLEIC ACIDS RESEARCH** held by our library in which the following articles appear:

Cotten, et al, **NUCLEIC ACIDS RESEARCH 1991**, 19(10):2629.

Wagner, et al., **NUCLEIC ACIDS RESEARCH 1991**, 19(21):5965.

The edition in which the Cotten, et al. reference appears was received by our library on June 6, 1991, and the edition in which the Wagner, et al. reference appears was received by our library on November 20, 1991.

Sincerely,

Valerie J. VanBilliard
Document Delivery Specialist

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